

REMARKS/ARGUMENTS

With this amendment, Claims 1-26 are pending. Claims 21-24 are withdrawn from consideration as being drawn to nonelected inventions. Claims 11-13 are canceled without prejudice to subsequent revival. For convenience, the Examiner's rejections are addressed in the order presented in the January 2, 2003 Office Action.

I. Status of the claims

Claims 1-20, 25 and 26 are under examination and are rejected. Claims 3 and 16 are amended to include stringent hybridization conditions. Support for this amendment is found, for example, at page 14, lines 9-20. This amendment adds no new matter.

Claims 1, 12, and 18 are amended to recite "wherein the Apop3 protein affects apoptosis." Support for this amendment is found, for example, at page 34, lines 18-21; in Example 6, page 46; and in Figure 9. This amendment adds no new matter.

Claim 25 is amended to recite "wherein said Apop3 protein affects apoptosis," and "determining the effect of the candidate bioactive agent on apoptosis, thereby determining the ability of the candidate bioactive agent to modulate the activity of the Apop3 protein." Support for this amendment is found, for example, at page 34, lines 7-23 and at Example 6, page 46, lines 9-20. This amendment adds no new matter.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 3, 16, 25, and 26 are rejected under 35 U.S.C. §112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter regarded by the Applicants as the invention. To the extent the rejection applies to the claims as amended, Applicants respectfully traverse the rejections.

Claims 3 and 16 are rejected as allegedly indefinite for reciting "hybridizes under high stringency condition" but not reciting hybridization conditions. Applicants have amended claims 3 and 16, to recite stringent hybridization conditions found in the specification at page 14, lines 9-20. This amendment adds no new matter.

Claims 25 and dependent claim 26 are rejected as indefinite for allegedly omitting essential steps. The Office Action states that a conclusion step linking step b and the preamble has been omitted. Applicants have amended claim 25 to read " a) adding a candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding said Apop3 protein, wherein said Apop3 protein affects apoptosis; and b) determining the effect of the candidate bioactive agent on apoptosis, thereby determining the ability of the candidate bioactive agent to modulate the activity of the Apop3 protein."

In view of the above amendments and remarks, Applicants respectfully request that the rejection for alleged indefiniteness be withdrawn.

III. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1, 3, 4, 6-12, 15-20, 25, and 26 were rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. The standard for enablement cited by the Examiner is that the specification must enable one skilled in the art to be able to make and use the invention commensurate in scope with the claims.

The Examiner appears to have focused improperly on inoperative embodiments, leading to the conclusion that undue experimentation would be required to identify biologically active peptides that carry out the methods of the claimed invention. However, the proper test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation" (*see, e.g.*, MPEP §2164.01). In the present application, one of skill would know how to avoid inoperative embodiments and

make biologically active polypeptides, without undue experimentation (*see, In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971)). Moreover, the present application provides guidance in the form of assays for identification of nucleic acids that encode of biologically active Apop3 proteins.

A. The specification teaches routine assays for identification of biologically active Apop3 proteins.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see, Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, “a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed” (*see, Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)).

As described above, the specification teaches routine methods for making biologically active Apop3 polypeptides. Furthermore, the specification also provides standard assays and working examples for identifying Apop3 polypeptides that affect apoptosis. Other related biological activities of Apop3 (*e.g.*, kinase activity, activation of caspase, and activation of NF- κ B) are also taught by the specification. Identification of biologically active Apop3 polypeptide is, therefore, well within the means of one of skill of the art, without undue experimentation. Assays for detection of apoptosis are found, for example, at page 35, lines 13-27, line 4 and in Example 6, page 46. Assays for kinase activity are found, for example, at page 34, lines 19-23 and Example 5, page 46. Assays for activation of caspase are found, for example, in Example 7 at page 47. Assays for NF- κ B activation are found, for example, at Example 8, pages 47-48.

B. One of skill in the art would know how to avoid inoperative embodiments.

Claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. As described by the court in *In re Cook and Merigold*, 169 USPQ 302:

Many patented claims read on vast numbers of inoperative embodiments in the trivial sense that they can and do omit 'factors which must be presumed to be within the level of ordinary skill in the art'.... There is nothing wrong with this so long as it would be obvious to one of ordinary skill in the relevant art how to include those factors in such a manner as to make the embodiment operative rather than inoperative.

See, In re Cook and Merigold, 169 USPQ at 302 (quoting in part *In re Skrivan*, 166 USPQ 85, 88 (C.C.P.A. 1970)).

The Office Action alleges that, to provide enablement, the specification must teach specific structures responsible for apoptosis. The Office Action also cites Wang *et al.* as showing that a single amino acid change can affect the activity of a specific enzyme, and that all such changes must be found in the specification. Applicants respectfully traverse. The specification and the knowledge of those of skill in the art provide guidance on amino acid changes that will likely be tolerated without affecting the activity of a protein.

The Examiner appears concerned that if one of skill in the art choose to modify the amino acid sequence of Apop3, the skilled artisan would likely choose to make an inoperative embodiment. The Examiner's concern is misplaced for the following reasons. 1) The specification provides guidance on amino acid changes that will likely be tolerated without affecting the activity of a protein. (*See e.g.*, specification at page 16, lines 13-38.) 2) The properties of amino acids are well known by those of skill in the art. Amino acids are characterized by their hydrophobicity, charge, and bulk of side chains, for example. Knowing the properties of particular amino acids, the skilled

artisan could easily choose appropriate amino acids to add to the core active sites and could avoid adding amino acids that would be detrimental to the structure or function of the polypeptide. In addition, those of skill in the art are aware of methods, like alanine scanning, where amino acid sequences are manipulated with minimal disruption of protein structure or function.

IV. Priority

The Office Action asserts that a priority application, USSN 60/099,468 (the '468 application), discloses Apop3 nucleic acid and the encoded protein, but alleges that the '468 application does not disclose how to use the products and thus, fails to provide adequate support for the claimed invention under 35 U.S.C. §112. Applicants respectfully traverse and assert that the '468 application teaches how to use the claimed invention, and thus a claim of priority to the '468 application is appropriate.

The '468 specification provides support for biological activity of Apop3, *e.g.*, ability to affect apoptosis, kinase activity, activation of NF- κ B, and activation of caspase-3. Specification at page 32, lines 15-21. The specification also discloses that cells into which Apop3 is introduced, normally undergo apoptosis. Specification at page 33, lines 11-12. The specification also teaches indicators of apoptosis at page 33, lines 16-21. Finally the specification also demonstrates that Apop3 activates NF- κ B and caspase-3. Activation of NF- κ B and caspases are known features of apoptosis. *See, e.g.*, specification at page 2, lines 1-17. Thus, the '468 application provides support for how to use the claimed invention.

Because the '468 application provides support for the claimed invention, *e.g.*, for Apop3 nucleic acids, proteins, and methods to use them, applicants respectfully request that the claim for priority under 35 U.S.C. 119(e) be allowed.

V. Rejections under 35 U.S.C. §102(e)

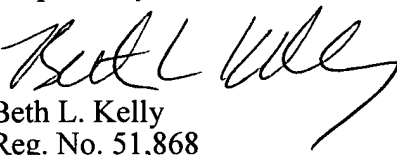
Claims 1-11, 19, and 20 are rejected under 35 U.S.C. §102(e) in view of US Patent No. 6,096,539 (the '539 patent); filed June 10, 1999. Claims 12-18, 25, and 26 are rejected under 35 U.S.C. §102(e) in view of US Patent No. 6,267,956 (the '956 patent); priority date June 10, 1999. Applicants respectfully traverse the rejection. As discussed above, the present application is fully supported by and claims priority to the '486 application, filed on September 8, 1998. Because the priority date of the present application is well before the filing or priority dates of the '539 and '956 patents, those patents are not properly cited as prior art. In view of priority date of the present application, Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


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